Stem Cell Programming With Chimeric Antigen Receptors to Eradicate HIV Infection

Grant Award Details

Stem Cell Programming With Chimeric Antigen Receptors to Eradicate HIV Infection

Grant Type: Early Translational IV

Grant Number: TR4-06845

Project Objective: The objective of this project is to generate a source of HIV-specific non-HLA restricted T cells that would target HIV infected cells. This would be accomplished by introducing novel CARs into CD34+ stem progenitor cells and Stem memory (Tscm) cells. The goal is to identify the development candidate--i.e. the best vector, best CAR construct and best cell candidate (CD34+ vs. Tscm).

Investigator:

Name: Zack Jerome

Institution: University of California, Los Angeles

Type: PI

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Name: Otto Yang

Institution: University of California, Los Angeles

Type: Co-PI

Disease Focus: HIV/AIDS, Infectious Disease

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: $4,925,166

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: NCE (Year 4)

View Report

Grant Application Details

Application Title: Stem Cell Programming With Chimeric Antigen Receptors to Eradicate HIV Infection

Public Abstract: The AIDS virus infects and destroys cells of the immune system such that the bodies of infected individuals cannot fight infections or some cancers. If untreated HIV infection leads to death. Current therapies to stop virus replication in the body are expensive and can have side effects. They also do not eliminate the virus from the body. Our overall goal is to use a gene therapy approach to improve a patient's own immune response against HIV, thus rendering them able to fight their own viral infection. We will test an approach designed to engineer a patient's immune system so that it can directly kill cells infected by HIV, thereby preventing spread of the virus throughout the body. This would decrease virus replication, and perhaps eliminate HIV from the body. This should prevent the HIV-induced destruction of the immune system, and restore the body's ability to mount immune responses against a variety of infectious agents and cancers, and may eliminate the need for the patient to take antiretroviral drugs. Successful completion of this project will yield an immunotherapeutic that is ready for preclinical development as a treatment for HIV-1 infection and AIDS.

Statement of Benefit to California: California ranks second in the nation in cases of HIV/AIDS, with over 155,000 persons living with HIV infection currently. This is projected to increase steadily to over 172,000 persons in the next 5 years. Aside from the personal, social, and work productivity losses due to HIV infection and its treatment, the direct healthcare cost to California is thought to approach $1.8 billion annually (CDC).

A curative treatment is therefore a high priority, given the high costs of chronic treatment and the increasingly apparent long-term toxicities of the antiretroviral drugs. Stem cell therapy offers promise for this goal, by addressing two major immune mechanisms of failure to control HIV infection: 1) loss of both anti-HIV CD8+ T-cells and the CD4+ T-cells required for their maintenance and function, and 2) CD8+ T-cell targeting that is subject to HIV evasion through mutation and down-modulation of the class I Human Leukocyte Antigens that present HIV protein sequences to CD8+ T-cells.

In this project, we propose to develop a strategy to program stem cells to provide a self-renewing population of both CD8+ and CD4+ HIV-targeted T-cells that are resistant to direct HIV infection, and which bypass the mechanisms by which HIV usually evades the immune response. If successful, this approach would allow development of a one-time stem cell gene therapy treatment that yields long-term immune control of HIV infection.